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23859 7590 01/14/2009

Ballard Spahr Andrews & Ingersoll, LLP
SUITE 1000
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ATLANTA, GA 30309-3915

EXAMINER	
NOAKES, SUZANNE MARIE	
ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 01/14/2009

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/634,027	08/04/2003	Artem Gennady Evdokimov	01279.0009U1	5050

TITLE OF INVENTION: THREE DIMENSIONAL COORDINATES OF HPTPBETA

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1510	$300	$0	$1810	04/14/2009

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

23859 7590 01/14/2009

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Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/634,027	08/04/2003	Artem Gennady Evdokimov	01279.0009U1	5050

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nonprovisional	NO	$1510	$300	$0	$1810	04/14/2009

EXAMINER	ART UNIT	CLASS-SUBCLASS
NOAKES, SUZANNE MARIE	1656	435-195000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:

❑ Issue Fee

❑ Publication Fee (No small entity discount permitted)

❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

❑ A check is enclosed.

❑ Payment by credit card. Form PTO-2038 is attached.

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

❑ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

❑ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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EXAMINER	
NOAKES, SUZANNE MARIE	
ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 01/14/2009

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 193 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 193 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

Notice of Allowability	Application No.	Applicant(s)	
	10/634,027	EVDOKIMOV ET AL.	
	Examiner	Art Unit	
	SUZANNE M. NOAKES	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the RCE filed 01/08/2009 and the previously agreed upon Ex, Amendments (see OA 12/31/08)*.

2. ☒ The allowed claim(s) is/are *26-33 and 35*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 01/08/2009
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 08 January 2009 has been entered.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on 08 January 2009 has been considered by the examiner. See initialed and signed PTO-1449.

3. The following is a reiteration of the previous Examiner's Amendment and Notice of Allowance mailed 31 December 2008. The references cited in the IDS above are all general references which in no way compromise the patentability of the previous/instant claim amendments.

EXAMINER'S AMENDMENT

4. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided

by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Richard Echler on 12 December 2008.

The application has been amended as follows:

In the claims:

CANCEL Claims 10-24.

25. (Currently Amended) A method of identifying a drug candidate compound for the treatment of an angiogenic mediated disorder, comprising:

a) employing the three-dimensional structural coordinates of the human protein tyrosine phosphatase beta **(**HPTPbeta**)** catalytic domain [SEQ ID NO:7] as set forth in Figures 202-252 to graphically image the HPTPbeta catalytic domain [SEQ ID NO :7], and determining the binding mode of a compound within the catalytic domain;

b) selecting one or more compounds which have ~~similar binding modes~~ the best fit with the HPTPbeta catalytic domain [SEQ ID NO:7] as set forth in Figures 202-252 wherein the compounds are computationally positioned at one or more areas of said imaged HPTPbeta catalytic domain [SEQ ID NO:7] and

c) assaying analyzing the ability of said drug candidate compound to bind or modulate HPTPbeta activity.

26. (Currently Amended) A method of identifying a drug candidate compound for the treatment of an angiogenic mediated disorder, comprising:

a) employing the three-dimensional structural coordinates of the HPTPbeta catalytic domain [SEQ ID NO:7] as set forth in Figures 7-102 to graphically image the HPTPbeta catalytic domain [SEQ ID NO:7], and determining the binding mode of a compound within the catalytic domain;

b) selecting one or more compounds which have ~~similar binding modes~~ the best fit with the HPTPbeta catalytic domain [SEQ ID NO:7] as set forth in Figures 7-102 wherein the compounds are computationally positioned positioning a drug candidato compound at one or more areas of said imaged HPTPbeta catalytic

domain [SEQ ID NO:7]; and

c) assaying the ability of said drug candidate compound to bind or modulate HPTPbeta activity.

27. (Previously Presented) The method according to claim 25, wherein said drug candidate compound is positioned at at least amino acid residues 152, 74-77, 209-214, 244-253, 288-290, and 293 of [SEQ ID NO:7].

28. (Previously Presented) The method according to claim 26, wherein said drug candidate compound is positioned at at least amino acid residues 152, 74-77, 209-214, 244-253, 288-290, and 293 of [SEQ ID NO:7].

29. (Previously Presented) The method according to claim 25, wherein said drug candidate compound is positioned at at least amino acid residues 76-80, 48-66, 284-292 and 212-214 of [SEQ ID NO:7].

30. (Previously Presented) The method according to claim 26, wherein said drug candidate compound is positioned at at least amino acid residues 76-80, 48-66, 284-292 and 212- 214 of [SEQ ID NO:7].

31. (Previously Presented) The method according to claim 25, wherein said drug candidate compound is positioned at at least amino acid residues 69-76, 119-123, and 149-154 of [SEQ ID NO:7].

32. (Previously Presented) The method according to claim 26, wherein said drug candidate compound is positioned at at least amino acid residues 69-76, 119-123, and 149-154 of [SEQ ID NO:7].

33. (Currently Amended) A method of identifying an inhibitor of an HPTPbeta molecule, comprising:

a) providing a crystal of HPTPbeta comprising the amino acid residues of SEQ ID NO:7 which either has space group $P2_12_12_1$ and unit cell parameters a=39Å, b= 72Å, c=120 Å and α=β=γ=90°, or space group $P2_1$ with unit cell parameters of a=62Å, b=70Å, c=70Å and α=90°, β=93°, γ=90°;

b) subjecting the crystal in (a) to X-ray diffraction and determining the three-dimensional structure coordinates of the HPTPbeta catalytic domain;

c) employing the three-dimensional structure coordinates from (b) to graphically display the three-dimensional structure and identifying the active binding site residues of Asn74 Asn75 Ile76, Leu77, Cys152, Pro209, Asp210, His211, Gly212, Va1213, Pro214, Cys244, Ser245, Ala246, Gly247, Va1248, Gly249, Arg250, Thr251, Gly252, Thr253, Gln288, Thr289, Glu290, and Tyr293;

~~b) determining the three-dimensional atomic coordinates of amino acids Asn74 Asn75 Ile76, Leu77, Cys152, Pro209, Asp210, His211, Gly212, Va1213, Pro214, Cys244, Ser245, Ala246, Gly247, Va1248, Gly249, Arg250, Thr251, Gly252, Thr253, Gln288, Thr289, Glu290, and Tyr293 of an active binding site of the HPTPbeta molecule by X-ray diffraction of the crystal;~~

~~[[c]]~~) d) using the atomic coordinates of amino acids Asn74 Asn75 Ile76, Leu77, Cys 152, Pro209, Asp210, His211, Gly212, Va1213, Pro214, Cys244, Ser245, Ala246, Gly247, Va1248, Gly249, Arg250, Thr251, Gly252, Thr253, Gln288, Thr289, Glu290, and Tyr293 as determined in c) to generate a three-dimensional structure of a molecule comprising an HPTPbeta active site binding pocket so that the root mean square deviation of conserved residue backbone atoms is less than 1.5 Å as compared to the three-dimensional coordinates in a-c)~~, to generate a three-dimensional structure of a molecule comprising an HPTPbeta active site binding pocket~~;

~~[[d]]~~) e) employing the three-dimensional structure from d) to design or select a potential drug candidate; and

~~[[e]]~~) f) contacting the potential drug candidate with the molecule to determine the ability of the potential inhibitor to associate with the molecule.

34. CANCEL

35. (Currently Amended) A method of identifying an inhibitor of an HPTPbeta molecule, comprising:

a) providing a crystal of HPTPbeta comprising the amino acid residues of SEQ ID NO:7 which either has space group $P2_12_12_1$ and unit cell parameters a=39Å, b= 72Å, c=120 Å and α=β=γ=90°, or space group $P2_1$ with unit cell parameters of a=62Å, b=70Å, c=70Å and α=90°, β=93°, γ=90°;

b) subjecting the crystal in (a) to X-ray diffraction and determining the three-dimensional structure coordinates of the HPTPbeta catalytic domain;

c) employing the three-dimensional structure coordinates from (b) to graphically display the three-dimensional structure and identifying the active binding site residues of Glu48, Glu49, Leu50, Lys51, Asp52, Va153, Gly54, Arg55, Asn56, Gln57, Ser58, Cys59, Asp60, Ile61, Ala62, Leu63, Leu64, Pro65, Glu66, Ile76, Leu77, Pro78, Tyr79, Asp80, Gly212, Va1213, Pro214, Va1284, His285, Met286, Va1287, Gln288, Thr289, Glu290, Cys291, and Gln292;

~~b) determining the three-dimensional atomic coordinates of amino acids Glu48, Glu49, Leu50, Lys51, Asp52, Va153, Gly54, Arg55, Asn56, Gln57, Ser58, Cys59, Asp60, Ile61, Ala62, Leu63, Leu64, Pro65, Glu66, Ile76, Leu77, Pro78, Tyr79, Asp80, Gly212, Va1213, Pro214, Va1284, His285, Met286, Va1287, Gln288, Thr289, Glu290, Cys291, and Gln292 of an active binding site of the HPTPbeta molecule by X-ray diffraction of the crystal;~~

~~[[c]]~~) d) using the atomic coordinates of amino acids Glu48, Glu49, Leu50, Lys51, Asp52, Va153, Gly54, Arg55, Asn56, Gln57, Ser58, Cys59, Asp60, Ile61, Ala62, Leu63, Leu64, Pro65, Glu66, Ile76, Leu77, Pro78, Tyr79, Asp80, Gly212, Va1213, Pro214, Va1284, His285, Met286, Va1287, Gln288, Thr289, Glu290, Cys291, and Gln292 as determined in c) to generate a three-dimensional structure of a molecule comprising an HPTPbeta active site binding pocket so that the root mean square deviation of conserved residue backbone atoms is less than 1.5 Å as compared to the three-dimensional coordinates in a-c)~~, to generate a three-dimensional structure of a molecule comprising an HPTPbeta active site binding pocket~~;

~~[[d]]~~) e) employing the three-dimensional structure from d) to design or select a potential drug candidate; and

~~[[e]]~~) f) contacting the potential drug candidate with the molecule to determine the ability of the potential inhibitor to associate with the molecule.

36. CANCEL.

Reasons for Allowance

5. The following is an examiner's statement of reasons for allowance: The claims are drawn to methods of identifying candidate drug compounds that bind to the catalytic domain of the human protein tyrosine phosphatase beta (HPTPbeta). The method utilizes *in silico* screening of candidate compounds by emplying the three-dimensional

structure of the catalytic domain of said HPTPbeta (SEQ ID NO: 7), which has been characterized by as two different three-dimensional structures (e.g. Figures 7-102 and Figures 202-252) both of which are apo- structures, wherein the former (Figures 7-102) is derived from monoclinic crystals, the later derived from othorhrombic crystals (Figures 202-252). The three-dimensional structures and specifically the noted and identified binding pocket residues as limited in the claims are not taught in the prior art nor are they obvious over the prior art. While the main focus in the prior art has centered around the well known human protein tyrosine phosphatase 1B protein, little is known about the catalytic binding pocket of the HPTPbeta enzyme. Thus, utilizing the structural coordinates as outlined in claims 25, 26, 33 and 35 are both novel and non-obvious over the art of record. **Thus, claims 26-33 and 35 are allowed**.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUZANNE M. NOAKES whose telephone number is (571)272-2924. The examiner can normally be reached on 7.00 AM-3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SUZANNE M. NOAKES/
Primary Examiner, Art Unit 1656
13 January 2009